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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/662,678
Filing Date: September 15, 2003
Appellant(s): TROUP ET AL.

ROBERT M. BARRETT
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed April 21, 2011 appealing from the Office action mailed November 24, 2010.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Claims 1-4, 7-11, 13-14, 16-17 and 23-28.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

6,077,828	ABBRUZZESE	6-2000
4,112,123	ROBERTS	9-1978
6,420,342	HAGEMAN	7-2002
6,953,679	SALVATI	10-2005
6,203,820	VICKERY	3-2001
2003/0119888	ALLEN	6-2003
4,544,568	HEYLAND	10-1985

Phillips, B. "Sports Supplement Review" 3rd issue, 1997, pp. 66-70.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-4, 7-11, 13-14, 16-17 and 23-28 stand rejected under 35 U.S.C. 103(a) as unpatentable over Abbruzzese et al (US Patent No. 6,077,828) as evidenced by Roberts (US Patent No. 4,112,123), in view of Hageman et al (US Patent No. 6,420,342) and Salvati et al (US Patent No. 6,953,679) and Vickery (US Patent No. 6,203,820).

Abbruzzese et al teach nutritional compositions for the prevention of cachexia and anorexia. The reference teaches a composition comprising effective amounts of ω-3 fatty acids, such as alpha-linolenic acid, stearidonic acid, eicosapentanenoic acid, docosapentaenoic acid, docosahexanoic acid or mixtures thereof; of branched-chain amino acids valine, leucine, isoleucine or mixtures thereof; with or without reduced

levels of tryptophan and 5-hydroxytryptophan; and of antioxidant system selected from the group consisting of beta-carotene, vitamin C, vitamin E, selenium or mixtures thereof (see abstract). The reference teaches a liquid nutritional composition comprising (a) at least 1000 mg per liter of ω-3 fatty acids, wherein the weight ratio of ω-6 fatty acids to ω-3 fatty acids is from about 0.1 to about 1.0; (b) at least 50 grams per liter of a source of amino nitrogen, wherein 15 to 50% by weight of the amino-nitrogen is branched-chain amino acids, and wherein tryptophan is present in an amount less than about 5.0% by weight of the total amino-nitrogen, and (c) at least 1 gram per liter of an antioxidant system comprising beta-carotene, vitamin C, vitamin E and selenium (see claim 1). The reference teaches that the total amount of branched-chain amino acids (“BCAA") useful in the present invention is about 15-50 g/100 g protein (i.e. percent), preferably about 15-25 g/100 g. Thus, an 8 oz. container of the nutritional composition would contain up to about 8 g BCAAs per 16 grams of total protein. The daily delivery of BCAAs is about 5-26 g (see column 9, lines 26-31). The reference teaches the branched-chain amino acids valine, leucine, isoleucine or mixtures thereof (see abstract). Therefore, since there is 9.08 g and total of 19.75 g of BCAA, 9.08/19.75 is about 46% of the leucine in the BCAA. Since the reference teaches that the total amount of BCAA useful in the present invention is about 15-50 g/100 g protein, and there is 46% of leucine in the BCAA composition, this implies that there is about 23% of leucine. Additionally, the reference teaches that the nutritional composition comprises branched-chain amino acids, valine, leucine, isoleucine or mixtures of thereof. Furthermore, the reference teaches that the liquid nutritional composition comprises per

liter (a) at least 0.45 gm (450 mg) of ω-3 fatty acids, (b) at least 50 grams of a source of amino-nitrogen wherein 15-50% by weight of the amino-nitrogen is branched-chain amino acids and wherein tryptophan is present in an amount less than about 5.0% of the total amino-nitrogen, and (c) at least 1 gram of an antioxidant (see column 4, lines 20-36). Therefore, if there was 46% of leucine present, and 46% of 50 gram is 23 grams of leucine present in the composition, this implies that there is about 46% of leucine present in the composition.

The reference further teaches that the composition comprises essential amino acids, such as lysine, isoleucine, methionine, phenylalanine, threonine, tryptophan, valine or histidine, and teaches the amino acid profile of a nutritional composition (see Table 4). Since there is at least about 36 g of essential and/or conditionally essential amino acids per serving and about 15-50 g of BCAA per 100 g of protein, this meets the limitation of claims 14 and 16. Furthermore, since the reference teaches that there is at least 50 grams of a source of amino-nitrogen wherein 15-50% by weight of the amino nitrogen is BCAA, and Table 4 indicates that 9.08 gram of leucine is present, according to the calculation above, this equals about 46% of BCAA. Thus, if 50% by weight of the amino nitrogen is BCAA, there is at least 25 grams of BCAA present. And if about 46% of BCAA is leucine, this implies that there is about 11.5 g of leucine present, meeting the limitation of claim 26. The reference teaches 2.78 g of methionine in 100 g of protein, meeting the limitation of at least about 0.5% to about 5% of methionine of claim 7, The reference teaches that the nutritional composition comprises vitamin E (tocopherol (all natural form or d1-alpha-tocopherol acetate) (see Table 6), meeting the

limitation of claim 11. The reference teaches that the EPA is in the amount of 1.09 g and DHA is in the amount of 0.46 g (see Table 3), meeting the limitation of claims 8-10. The reference further teaches that for treatment of ulcerative colitis, compositions include a protein source that can be intact or hydrolyzed proteins of high biological value (see column 3, lines 1-5) and teaches 75% whey protein concentrate as one of the ingredients (see table 7). Furthermore, since the reference teaches a whey protein concentrate, this protein would inherently comprise essential and conditionally essential amino acid profiled, thus meeting the limitation of range from about 0.60 to about 0.90 amino acids.

As evidenced by Roberts (US Patent No. 4,112,123), per 100 g of whey protein, there is 13.0 g of leucine (see Table 1). Since there is at least 9.08 g of leucine to 13.0 g of leucine in 100 g or whey protein, this would meet the limitation of ratio of 1:3 to 3:1. Furthermore, the reference teaches that for example, the daily nutritional management of liver cancer includes administration of 2 to 4 containers of 8 ounces servings (237 mL) of the nutritional composition providing a daily amount of (i) combined EPA and DHA in the range of 3 to 6 g (preferred dosage 3 g), (ii) BCAA in the range of 5 to 25 g (preferred dosage about 10-15 g), (iii) vitamin C in the range of 125 to 500 mg (preferred about 300 mg), (iv) vitamin E (tocopherol) in the range of 50 to 250 IU (preferred 150 IU), (v) beta-carotene in the range of 1250 to 3250 μg (preferred 2500 μg), (vi) selenium in the range of 40 to 60 μg (preferred about 45 μg). The reference teaches that for cancer cachexia and anorexia, the effect of nutritional intervention are monitored at monthly intervals as known in the art, and depending on the results

obtained, the therapeutic regimen is developed to maintain and/or boost the weight gain by the patient (see column 15, lines 44-65, Example III). The mass equivalents of 1 IU for vitamin E is 0.667 mg d-alpha-tocopherol, or of 1 mg of d1-alpha-tocopherol acetate (definition of IU from medicinenet.com). Therefore, 50 to 250 IU would equal to 33.55 mg to 167.75 mg of tocopherol, meeting the limitation of claim 13.

The difference between the reference and the instant claims is that the reference does not teach at least 30% by weight of leucine based on the weight of intact protein, valine in an amount of about 8% to about 10% by weight of total amino acids, a kit comprising a first composition and a second composition comprising an anti-cancer drug, wherein said anticancer drug is 5-fluorouracil, mitomycin-C, adriamycin, chloroethyl nitrosureas or methotrexate, and that the methionine in free and/or salt from is in an amount of at least about 5% to about 7% by weight on the weight of total amino acids.

However, Hageman et al teach a nutritional, pharmaceutical or dietetic preparation can be manufacture in dry form, as bar, as powder, as tablet, and cookie or as cereal (see column 5, lines 60-63). The reference teaches for products for sportsmen the following mixtures of amino acids appeared to be especially beneficial for muscle growth, when consumed in an amount of more than 2 and preferably more than 4 g per daily dose: 3-10 wt% histidine, 5-15% isoleucine, 10-23% % leucine, 10-23% lysine, 5-15% methionine, 5-15 wt % phenylalanine, and 5-15 wt % threonine (see column 6, lines 59-67 and column 7, line 1). Furthermore, the reference teaches that when proteins are included in the nutritional preparations, the amount that is included

depends on the application (see column 6, lines 39-41) and the proteins are proteins of dairy, vegetable or animal origin, such as skimmed milk powder, whey powder, egg white powder, potato protein, soy protein, etc., or hydrolysates, or mixtures thereof (see column 6, lines 27-32). The reference teaches that when proteins are included in the nutritional preparation, the amount that is included depends on the application of the product. In complete formula typically an amount of 5-120 g per daily dose…for young infants the amount will be in the range 5-15 g per daily dose...in complete enteral nutrition for feeding surgery patients, typically 50-120 g per daily dose…In supplement typically 0-60 g protein per daily dose will be included (see column 6, lines 39-50). In regards to claim 25, the claim is drawn to "a composition consisting essentially of..." In regards to claim 27, the claim is drawn to "a kit comprising: a first composition consisting essentially of..." Applicant has not defined what encompasses "consisting essentially of" in the specification. In fact the instant specification does not define the phrase "consisting essentially of". The MPEP states the following: "The transitional phrase ‘consisting essentially of’ limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. A ‘consisting essentially of’ claim occupies the middle ground between closed claims that are written in a consisting of’ format and fully open claims that are drafted in a comprising' format...For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of” will be construed as equivalent to 'comprising'" (see MPEP 2105). Therefore, claims

25 and 28 have been treated as “a composition comprising…” the same claim language as original claim 3.

Furthermore, Salvati et al teach a fused cyclic compound and the use of the fused cyclic compound with a nutritional supplements in combination with whey protein or casein, amino acids (such as leucine, branched amino acid and hydroxymethylbutyrate), triglycerides, vitamins (e.g., A, B6, B12, folate, C, D, and E), minerals, etc. (see column 45, lines 48-56). Furthermore, the reference teaches anti-proliferative agents for use in combination with the compounds such as adriamycin (see column 45, lines 41-43) and anti-cancer agents, such as methotrexate, 5-fluorouracil (see column 46, lines 64-67). The reference teaches a kit comprising a first container (such as a vial) containing a pharmaceutical formulation comprising a compound, a second container (such as a vial) containing a pharmaceutical formulation comprising one or more agents to be used in combination with the compound of the invention (see 47, lines 55-64).

Additionally, Vickery et al teach a composition for enhancing protein anabolism, and nutritional composition comprising L-arginine, L-cysteine, L-histidine, L-isoleucine, L-leucine, L-lysine, L-methionine, L-phenylalanine, L-threonine, L-tryptophan, L-tyrosine, and L-valine (see abstract and claim 1). Vickery teaches that L-leucine is useful in for lowering blood sugar, stimulating protein synthesis in muscle and wound healing of skin and bone (see column 3, lines 51-54). Vickery teaches that L-valine aids in wound healing, muscle growth and liver diseases. L-valine is present in the composition in an amount of from about 7% to about 10% by weight, from about 8% to

about 9% by weight (see column 2, lines 12-30 and column 4, lines 48-53, and claims 18 and 20-21).

Therefore, it would have been obvious for one of ordinary skill in the art to combine the teachings of Abbruzzese et al, Hageman et al and Salvati et al and Vickery reference to produce a kit comprising the anti-cancer agent with the nutritional composition, since all of the prior art teach nutritional composition. Salvati et al teach a kit comprising fused cyclic compound, nutritional supplement comprising leucine, whey and protein and any anti-cancer agent and Hageman et al and Abbruzzese et al and Vickery teach a nutritional composition comprising different amounts of amino acids. One of ordinary skill in the art would be motivated to combine, since Salvati et al teaches such a composition/kit. Furthermore, the composition taught in Abbruzzese, Hageman, and Salvati and Vickery can be used for the same purpose, for administering nutritional composition for such patients as cancer patients for enhancing protein anabolism and muscle enhancement. As evidenced by the instant specification, the compositions of the instant application are for the promotion of muscle protein synthesis and control of tumor-induced weight loss in patients that are, for example, suffering from cancer cachexia (see abstract). Furthermore, one of ordinary skill in the art would have been motivated to optimize the concentrations of the leucine and methionine and valine, since “it is the normal desire of scientist or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is optimum combination of percentages”. The MPEP states: Generally, differences in concentration or temperature will not support the patentability

of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. *"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."* *In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)* (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("*The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.*"); *In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969)* (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Furthermore, Abbruzzese patent '828 teaches that the effect of nutritional intervention on cancer cachexia and anorexia are monitored as known in the art, and depending on the results obtained, the therapeutic regimen is developed to maintain and /or boost weight gain by

the patient, with the ultimate goal of achieving tumor regression and complete eradication of cancer cells (see column 15, lines 57-64). Therefore, there is a reasonable expectation of success to optimize the concentrations of the essential amino acid/ leucine/ methionine, since it is "the normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages" and one of ordinary skill in the art would experiment with different concentrations to produce the optimal product. Due to the loss of appetite due to cancer treatment, and due to appetite suppression, nutrition is necessarily a part of treatment process for improving patient's everyday life. For the process of improving and treating cancer and loss of appetite due to cancer, a nutritional requirement would be optimized and adjusted accordingly by those skilled in the art. Abbruzzese teaches that the therapeutic regimen will be developed to maintain and/or boost weight gain, giving motivation to optimize the nutritional content. From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention. Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary. There is a reasonable expectation of success, since Salvati et al teach a kit that can comprise any agent, nutritional supplement for the treatment of cancer (prostate), and Hageman et al and Abbruzzese et al teach a nutritional supplement comprising essential amino acids that is useful in treating variety of diseases, including cancer, and Vickery teaches a nutritional composition comprising essential amino acid,

including leucine, valine, isoleucine and methionine to enhance protein anabolism and enhancing muscle growth and protein synthesis in the muscle.

Claims 1-4, 7-11, 13-14, 16 and 23-26 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Abbruzzese et al (US Patent No. 6,077,828, filed with IDS) as evidenced by Roberts (US Patent No. 4,112,123), in view of Allen et al (US 2003/0119888 A1) and Phillips Bill (Sports Supplement Review, 1997, pp. 66-70) and Vickery (US Patent No. 6,203,820).

Abbruzzese et al teach nutritional compositions for the prevention of cachexia and anorexia. The reference teaches a composition comprising effective amounts of ω-3 fatty acids, such as alpha-linolenic acid, stearidonic acid, eicosapentanenoic acid, docosapentaenoic acid, docosahexanoic acid or mixtures thereof; of branched-chain amino acids valine, leucine, isoleucine or mixtures thereof; with or without reduced levels of tryptophan and 5-hydroxytryptophan; and of antioxidant system selected from the group consisting of beta-carotene, vitamin C, vitamin E, selenium or mixtures thereof (see abstract). The reference teaches a liquid nutritional composition comprising (a) at least 1000 mg per liter of ω-3 fatty acids, wherein the weight ratio of ω-6 fatty acids to ω-3 fatty acids is from about 0.1 to about 1.0; (b) at least 50 grams per liter of a source of amino nitrogen, wherein 15 to 50% by weight of the amino-nitrogen is branched-chain amino acids, and wherein tryptophan is present in an amount less than about 5.0% by weight of the total amino -nitrogen, and (c) at least 1 gram per liter of an antioxidant system comprising beta-carotene, vitamin C, vitamin E and selenium (see

claim 1). The reference teaches that the total amount of branched-chain amino acids ("BCAA") useful in the present invention is about 15-50 g/100 g protein (i.e. percent), preferably about 15-25 g/100 g. Thus, an 8 oz. container of the nutritional composition would contain up to about 8 g BCAAs per 16 grams of total protein. The daily delivery of BCAAs is about 5-26 g (see column 9, lines 26-31). The reference teaches the branched-chain amino acids valine, leucine, isoleucine or mixtures thereof (see abstract). Therefore, since there is 9.08 g and total of 19.75 g of BCAA, 9.08/19.75 is about 46% of the leucine in the BCAA. Since the reference teaches that the total amount of BCAA useful in the present invention is about 15-50 g/100 g protein, and there is 46% of leucine in the BCAA composition, this implies that there is at least about 23% of leucine. Additionally, the reference teaches that the nutritional compositions comprises branched-chain amino acids, valine, leucine, isoleucine or mixtures of thereof. As evidenced by Roberts (US Patent No. 4,112,123), per 100 g of whey protein, there is 13.0 g of leucine (see Table 1). Since there is at least 9.08 g of leucine to 13.0 g of leucine in 100 g or whey protein, this would meet the limitation of ratio of 1:3 to 3:1.

Furthermore, the reference teaches that the liquid nutritional composition comprises per liter (a) at least 0.45 gm (450 mg) of ω-3 fatty acids, (b) at least 50 grams of a source of amino-nitrogen wherein 15-50% by weight of the amino-nitrogen is branched-chain amino acids and wherein tryptophan is present in an amount less than about 5.0% of the total amino-nitrogen, and (c) at least 1 gram of an antioxidant (see column 4, lines 20-36). Therefore, if there was 46% of leucine present, and 46% of 50

gram is 23 grams of leucine present in the composition, this implies that there is about 46% of leucine present in the composition.

The reference further teaches that the composition comprises essential amino acids, such as lysine, isoleucine, methionine, phenylalanine, threonine, tryptophan, valine or histidine, and teaches the amino acid profile of a nutritional composition (see Table 4). Since there is at least about 36 g of essential and/or conditionally essential amino acids per serving and about 15-50 g of BCAA per 100 g of protein, this meets the limitation of claims 14 and 16. Furthermore, since the reference teaches that there is at least 50 grams of a source of amino-nitrogen wherein 15-50% by weight of the amino nitrogen is BCAA, and Table 4 indicates that 9.08 gram of leucine is present, according to the calculation above, this equals about 46% of BCAA. Thus, if 50% by weight of the amino nitrogen is BCAA, there is at least 25 grams of BCAA present. And if about 46% of BCAA is leucine, this implies that there is about 11.5 g of leucine present, meeting the limitation of claim 26. The reference teaches 2.78 g of methionine in 100 g of protein, meeting the limitation of at least about 0.5% to about 5% of methionine of claim 7.

The reference further teaches that the nutritional composition comprises vitamin E (tocopherol (all natural form or d1-alpha-tocopherol acetate) (see Table 6), meeting the limitation of claim 11. The reference teaches that the EPA is in the amount of 1.09 g and DHA is in the amount of 0.46 g (see Table 3), meeting the limitation of claims 8-10. The reference further teaches that for treatment of ulcerative colitis, compositions include a protein source that can be intact or hydrolyzed proteins of high biological

value (see column 3, lines 1-5) and teaches 75% whey protein concentrate as one of the ingredients (see table 7). Furthermore, since the reference teaches a whey protein concentrate, this protein would inherently comprise essential and conditionally essential amino acid profiled, thus meeting the limitation of range from about 0.60 to about 0.90 amino acids. Furthermore, the reference teaches that for example, the daily nutritional management of liver cancer includes administration of 2 to 4 containers of 8 ounces servings (237 mL) of the nutritional composition providing a daily amount of (i) combined EPA and DHA in the range of 3 to 6 g (preferred dosage 3 g), (ii) BCAA in the range of 5 to 25 g (preferred dosage about 10-15 g), (iii) vitamin C in the range of 125 to 500 mg (preferred about 300 mg), (iv) vitamin E (tocopherol) in the range of 50 to 250 IU (preferred 150 IU), (v) beta-carotene in the range of 1250 to 3250 μg (preferred 2500 μg), (vi) selenium in the range of 40 to 60 μg (preferred about 45 μg). The reference teaches that for cancer cachexia and anorexia, the effect of nutritional intervention are monitored at monthly intervals as known in the art, and depending on the results obtained, the therapeutic regimen is developed to maintain and/or boost the weight gain by the patient (see column 15, lines 44-65, Example III). The mass equivalents of 1 IU for vitamin E is 0.667 mg d-alpha-tocopherol, or of 1 mg of d1-alpha-tocopherol acetate (definition of IU from medicinenet.com). Therefore, 50 to 250 IU would equal to 33.55 mg to 167.75 mg of tocopherol, meeting the limitation of claim 13. The difference between the reference and the instant claims is that the reference does not teach at least 30% to about 95% by weight of leucine and about 8% to about 10% valine.

However, Allen teaches that maintaining muscle mass while minimizing the accumulation of fat has long been an issue of concern to athletes. Food and/or vitamin supplements, as well as pituitary growth hormone, are necessary for muscle growth. Such ergogenic aids, that is supplements which stimulate muscle growth, include the three amino acids, leucine, isoleucine and valine (see paragraph [0004]). Furthermore, Phillips (1997) teaches that beta-hydroxy beta-methylbutyrate (HMB) is a metabolite of the essential amino acid leucine (see p. 66, “What is HMB?”). Phillips teaches that HMB up-regulate the ability to build muscle and burn fat, and may help decrease stress-induced muscle protein breakdown, and enhance increases in both muscle size and strength (see p. 66, “What do the scientific studies show?").

Additionally, Vickery et al teach a composition for enhancing protein anabolism, and nutritional composition comprising L-arginine, L-cysteine, L-histidine, L-isoleucine, L-leucine, L-lysine, L-methionine, L-phenylalanine, L-threonine, L-tryptophan, L-tyrosine, and L-valine (see abstract and claim 1). Vickery teaches that L-leucine is useful in for lowering blood sugar, stimulating protein synthesis in muscle and wound healing of skin and bone (see column 3, lines 51-54). Vickery teaches that L-valine aids in wound healing, muscle growth and liver diseases. L-valine is present in the composition in an amount of from about 7% to about 10% by weight, from about 8% to about 9% by weight (see column 2, lines 12-30 and column 4, lines 48-53, and claims 18 and 20-21).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings and optimize the amount of leucine and valine in the composition

to enhance the muscle performance. One of ordinary skill in the art would have been motivated to optimize the amount of leucine and valine in the composition, since Allen teaches that leucine, isoleucine and valine are three amino acids that stimulate muscle growth, Phillips teaches that leucine breaks down into HMB that build muscle, burn fat, and increases in both muscle size and strengths, and Vickery teaches that L-leucine is useful in for lowering blood sugar, stimulating protein synthesis in muscle and wound healing of skin and bone. Vickery teaches that L-valine aids in wound healing, muscle growth and liver diseases. L-valine is present in the composition in an amount of from about 7% to about 10% by weight, from about 8% to about 9% by weight. One would be motivated to give leucine to produce the down-stream compound HMB and valine to aid in muscle growth. Again, Leu, Ile and Val are well known to be used for stimulating muscle growth. The MPEP states that "Similarly, a prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. *Titanium Metals Corp of America v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985)." See MPEP 2144.05. The artisan would have expected Leu to behave the same at 25 or 30 or 35. Applicant's own example 4 shows clearly that Leu does not improve muscle building. The amount of protein synthesis and protein breakdown for both 25% leucine and 35% leucine was about the same for both leucine concentrations (see Table 4 of instant specification). Therefore, the differing concentrations of leucine would function the same. It appears that the additional components are important to the reduction of breakdown (see Table 4 of instant specification).

Furthermore, the MPEP further states: Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. *"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."* *In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)* (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("*The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.*"); *In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969)* (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Knowing that leucine, isoleucine and valine stimulate muscle growth, it would have been obvious to one or ordinary skill in the art to

optimize the concentrations of leucine, isoleucine or valine to enhance the muscle growth. Furthermore, since leucine produces the down-stream compound of HMB that is important in muscle growth and stimulation, it would have been obvious to optimize the concentration of leucine to produce the optimal composition. From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Claims 1 and 23-25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Heyland et al (US Patent No. 4,544,568) in view of Vickery (US Patent No. 6,203,820).

Heyland et al teach a composition comprising a 16 kg of technical leucine and 15 kg of whey powder (see column 5, lines 34-36). The reference teaches that technical leucine comprises a dry matter content of 99.6% and containing 65% of pure leucine, 13% of Cl^-, 18% of isoleucine and 2% of valine, the remainder consisting primarily of ash and phenylalanine (see column 5, lines 24-28). The reference teaches a composition comprising 150 g technical leucine, and 180 g whey powder (see Examples 2 and 3). This implies that per 150 g of technical leucine, there is 97.5 g of leucine, 27 g of isoleucine, 3 g of valine and about 3 g of phenylalanine. Therefore, 97.5 g leucine / 180 g whey protein gives 54.2% leucine. The difference between the reference and the instant claims is that the reference does not teach about 8% to about 10% valine.

However, Vickery et al teach a composition for enhancing protein anabolism, and nutritional composition comprising L-arginine, L-cysteine, L-histidine, L-isoleucine, L-leucine, L-lysine, L-methionine, L-phenylalanine, L-threonine, L-tryptophan, L-tyrosine, and L-valine (see abstract and claim 1). Vickery teaches that L-leucine is useful in for lowering blood sugar, stimulating protein synthesis in muscle and wound healing of skin and bone (see column 3, lines 51-54). Vickery teaches that L-valine aids in wound healing, muscle growth and liver diseases. L-valine is present in the composition in an amount of from about 7% to about 10% by weight, from about 8% to about 9% by weight (see column 2, lines 12-30 and column 4, lines 48-53, and claims 18 and 20-21).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of the prior arts because all references teach nutritional compositions comprising differing amounts of protein and essential amino acids (such as leucine) for the same purpose (muscle enhancement). One of ordinary skill in the art would be motivated to optimize the amounts of valine and isoleucine, since Vickery teaches that L-valine aids in wound healing, muscle growth and L-leucine is important in lowering blood sugar, stimulating protein synthesis in muscle and wound healing of skin and bond. Leu, Ile and Val are well known to be used for stimulating muscle growth. Vickery teaches about 7% to about 10% of leucine along with other amino acid compositions.

Furthermore, the MPEP further states: Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical.

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)* (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("*The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.*"); *In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969)* (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Knowing that leucine, isoleucine and valine stimulate muscle growth, it would have been obvious to one or ordinary skill in the art to optimize the concentrations of leucine, isoleucine or valine to enhance the muscle growth. From the teachings of the references, it is apparent that one of the ordinary

skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

(10) Response to Argument

Claims 1-4, 7-11, 13-14, 16-17 and 23-28 are unpatentable over Abbruzzese et al as evidenced by Roberts in view of Hageman et al and Salvati et al and Vickery references.

Appellant argues that "Appellant has surprisingly found that a formulation containing free essential amino acids as compared to a formulation containing free essential and non-essential amino acids or intact protein is optimal…In addition, Appellant has surprisingly and unexpectedly found that particularly useful compositions for promotion of muscle protein synthesis or controlling tumor-induced weight loss, such as cachexia, e.g. cancer cachexia may be obtained by combining essential amino acids in free form and/or in salt form with intact protein." Appellant argues that "Abbruzzese, Roberts, Hageman, Salvati and Vickery all fail to disclose or suggest compositions having leucine, valine in an amount of about 8% to about 10% by weight based on the weight of total amino acids, and at least one essential amino acid selected from the histidine, and combinations thereof in free and/or salt form, wherein said leucine, in free and/or salt form as required, in part, by independent claims 1-3, 17, 23-25 and 28."

Appellant argues that "Abbruzzese is directed to methods and nutritional compositions for preventing and treating cachexia and anorexia...at no place in the disclosure odes Abbruzzese disclose or suggest compositions containing about 8% to about 10% of valine as required, in part, by the present claims...at best, Abbruzzese discloses only 5.9% valine." Appellant further argues that "At no place in the disclosure does Hageman disclose or suggest compositions containing about 8% to about 10% of valine as required, in part, by the present claims…at best, Hageman discloses only 3.5% valine." Appellant further argues that "At no place in the disclosure does Salvati nor Roberts nor Vickery disclose or suggest compositions containing about 8% to about 10% of valine as required, in part, by the present claims. Furthermore, Appellant argues that "Vickery expressly discloses that valine may be present in an amounts of about 7% to about 10% based on the total weight of the composition…Vickery further defines the active ingredients as including various amino acids, molybdenum, creatinine, creatine, monohydrate, sulfur, methylsulfonylmethane, powdered egg white or powdered milk, and powdered enzymes."

Examiner respectfully asserts that Abbruzzese et al as evidenced by Roberts in view of Hageman et al and Salvati et al and Vickery references teach all of the components of the claimed nutritional composition. The primary reference teaches all of the active components of instant claims. The claims only require that valine in an amount of about 8% to about 10% by weight based on the weight of total amino acids, and at least 30% to about 95% by weight of leucine be present based on the weight of

total amino acids or weight of intact protein. The prior arts meet this limitation. As described in the body of the rejection, the reference teaches a liquid nutritional composition comprising (a) at least 1000 mg per liter of ω-3 fatty acids, wherein the weight ratio of ω-6 fatty acids to ω-3 fatty acids is from about 0.1 to about 1.0; (b) at least 50 grams per liter of a source of amino nitrogen, wherein 15 to 50% by weight of the amino-nitrogen is branched-chain amino acids, and wherein tryptophan is present in an amount less than about 5.0% by weight of the total amino -nitrogen, and (c) at least 1 gram per liter of an antioxidant system comprising beta-carotene, vitamin C, vitamin E and selenium. The reference teaches that the total amount of branched-chain amino acids (“BCAA") useful in the present invention is about 15-50 g/100 g protein (i.e. percent), preferably about 15-25 g/100 g. The reference teaches that the daily delivery of BCAAs is about 5-26 g. The reference teaches the branched-chain amino acids valine, leucine, isoleucine or mixtures thereof. Since there is 9.08 g of leucine and total of 19.75 g of BCAA, 9.08/19.75 is about 46% of the leucine in the BCAA. Since the reference teaches that the total amount of BCAA useful in the present invention is about 15-50 g/100 g protein, and there is 46% of leucine in the BCAA composition, this implies that there is about 23% of leucine.

Hageman et al teach products for sportsmen the following mixtures of amino acids appeared to be especially beneficial for muscle growth, when consumed in an amount of more than 2 and preferably more than 4 g per daily dose: 3-10 wt% histidine, 5-15% isoleucine, 10-23% % leucine, 10-23% lysine, 5-15% methionine, 5-15 wt % phenylalanine, and 5-15 wt % threonine. Furthermore, Salvati et al teach a fused cyclic

compound and the use of the fused cyclic compound with a nutritional supplements in combination with whey protein or casein, amino acids (such as leucine, branched amino acid and hydroxymethylbutyrate), triglycerides, vitamins (e.g., A, B6, B12, folate, C, D, and E), minerals, etc. Salvati teaches anti-proliferative agents for use in combination with the compounds such as Adriamycin, and anti-cancer agents, such as methotrexate, 5-fluorouracil. The reference teaches a kit comprising a first container (such as a vial) containing a pharmaceutical formulation comprising a compound, a second container (such as a vial) containing a pharmaceutical formulation comprising one or more agents to be used in combination with the compound of the invention.

Allen and Phillips teach the importance of leucine, isoleucine and valine in stimulating muscle growth. Vickery teaches that L-leucine is useful for lowering blood sugar, stimulating protein synthesis in muscle and wound healing of skin and bone. Vickery teaches that L-valine aids in wound healing, muscle growth and liver diseases. L-valine is present in the composition in an amount of from about 7% to about 10% by weight, from about 8% to about 9% by weight. Vickery reference teaches a composition comprising about 6% to about 9% L-arginine, about 2% to about 4% L-cystine, about 1.5% to about 3.5% L-histidine, about 6% to about 9% L-isoleucine, about 8% to about 12% L-leucine, about 6% to about 8% L-lysine, about 2.5% to about 4.5% L-methionine, about 5.5% to about 7.5% L-phenylalanine, about 4.5% to about 6.5% L-threonine, about 4% to about 6% L-tyrosine, about 7% to about 10% L-valine, about 0.001% to about 0.03% by weight molybdenum, about 3% to about 30% by weight creatine monohydrate, and about 5% to about 45% by weight methylsulfonylmethane (see

column 2, lines 8-30). When the least % of all components are added up, the molybdenum, creatine and methylsulfonylmethane would add up to about 10%. If there is about 7 to 9% L-valine, then there is about 7.8% (about 8%) L-valine based on the weight of total amino acids. Therefore, Vickery teaches the instant L-valine amount recited in the instant claims.

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings because all references teach nutritional compositions comprising differing amounts of protein and essential amino acids (such as leucine) for the same purpose (muscle enhancement). Salvati reference teaches combining antiproliferative agents for use in combination with the compounds and a kit containing the pharmaceutical formulation. Furthermore, the composition taught in Abbruzzese, Hageman, and Salvati can be used for the same purpose, for administering nutritional composition for such patients as cancer patients. Vickery reference teaches a nutritional composition and composition for enhancing protein anabolism. It would have been obvious to one of ordinary skill in the art to optimize the different amino acid concentration, especially leucine, since it is well known in the art that leucine, isoleucine and valine play an important role in muscle enhancement. As evidenced by the instant specification, the compositions of the instant application are for the promotion of muscle protein synthesis and control of tumor-induced weight loss in patients that are, for example, suffering from cancer cachexia (see abstract). Due to the loss of appetite due to cancer treatment, and due to appetite suppression, nutrition is necessarily a part of treatment process for improving patient's everyday life. For the process of improving

and treating cancer and loss of appetite due to cancer, a nutritional requirement would be optimized and adjusted accordingly by those skilled in the art. Abbruzzese teaches that the therapeutic regimen will be developed to maintain and/or boost weight gain, giving motivation to optimize the nutritional content. From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention. Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary. There is a reasonable expectation of success, since Salvati et al teach a kit that can comprise any agent, nutritional supplement for the treatment of cancer (prostate), and Hageman et al and Abbruzzese et al teach a nutritional supplement comprising essential amino acids that is useful in treating variety of diseases, including cancer. Both Allen and Phillips references were utilized to show the important role leucine plays in muscle enhancement. Vickery reference teaches the importance of L-valine and the composition comprising about 8 to about 12% leucine along with other amino acids.

In response to Appellant's argument regarding "surprising and unexpected benefits of the claimed composition having optimal amount of leucine and essential amino acids," Appellant has not compared the results of the instant components to the components of prior arts. The specification discloses that protein synthesis in muscle in Leu (25%) was 6.8 ± 1.1; Leu(35%) was 6.9 ± 0.6; Leucine alone was 6.6 ± 0.7. Protein breakdown in Leu (25%) was 8.1 ± 1.2; Leu (35%) was 8.0 ± 0.4; Leucine alone was 9.2 ± 0.5 (see Table 4). There is not much difference between Leu (25%) and Leu (35%)

and Leu alone for protein synthesis. There is not much difference between Leu (25%) and Leu (35%) for protein breakdown.

It is known in the art that that supplements which stimulate muscle growth, include the three amino acids, leucine, isoleucine and valine (see paragraph [0004] in Allen reference). Furthermore, Phillips (1997) teaches that beta-hydroxy beta-methylbutyrate (HMB) is a metabolite of the essential amino acid leucine (see p. 66, “What is HMB?”). Phillips teaches that HMB up-regulate the ability to build muscle and burn fat, and may help decrease stress-induced muscle protein breakdown, and enhance increases in both muscle size and strength (see p. 66, “What do the scientific studies show?"). Therefore, one of ordinary skill in the art would have been motivated to optimize the concentration of different amino acids, specifically leucine, isoleucine and valine to stimulate muscle growth, to arrive at the optimal composition for the treatment of muscle enhancement for cancer patients.

Claims 1-4, 7-11, 13-14, 16 and 23-26 are unpatentable over Abbruzzese et al as evidenced by Roberts in view of Allen et al and Phillips Bill and Vickery references.

Appellant argues that “Abbruzzese, Roberts, Allen, Phillips and Vickery all fail to disclose or suggest compositions having leucine, valine in an amount of about 8% to about 10% by weight based on the weight of total amino acids, and at least one essential amino acid selected from the histidine, and combinations thereof in free and/or salt form, wherein said leucine, in free and/or salt form as required, in part, by

independent claims 1-3, 17, 23-25 and 28." Appellant argues that "Abbruzzese is directed to methods and nutritional compositions for preventing and treating cachexia and anorexia...at no place in the disclosure odes Abbruzzese disclose or suggest compositions containing about 8% to about 10% of valine as required, in part, by the present claims...at best, Abbruzzese discloses only 5.9% valine." Appellant further argues that "At no place in the disclosure does Roberts disclose or suggest compositions containing about 8% to about 10% of valine as required, in part, by the present claims." Appellant further argues that "At no place in the disclosure does Allen disclose or suggest compositions containing about 8% to about 10% of valine as required, in part, by the present claims." Appellant argues that "Phillips is cited solely for the teaching that beta-hydroxy beta-methylbutyrate (HMB) is a metabolite of leucine and may help to build muscle…At no place in the disclosure does Phillips disclose or suggest compositions containing about 8% to about 10% 10% valine as required, in part, by the present claims." Furthermore, Appellant argues that "Vickery expressly discloses that valine may be present in an amounts of about 7% to about 10% based on the total weight of the composition…Vickery still fails to disclose or suggest the presently claimed amounts of valine."

Examiner respectfully asserts that Abbruzzese et al as evidenced by Roberts in view of Allen, Phillips and Vickery references teach all of the components of the claimed nutritional composition. The primary reference teaches all of the active components of instant claims. The claims only require that valine in an amount of about 8% to about

10% by weight based on the weight of total amino acids, and at least 30% to about 95% by weight of leucine be present based on the weight of total amino acids or weight of intact protein. The prior arts meet this limitation. As described in the body of the rejection, the reference teaches a liquid nutritional composition comprising (a) at least 1000 mg per liter of ω-3 fatty acids, wherein the weight ratio of ω-6 fatty acids to ω-3 fatty acids is from about 0.1 to about 1.0; (b) at least 50 grams per liter of a source of amino nitrogen, wherein 15 to 50% by weight of the amino-nitrogen is branched-chain amino acids, and wherein tryptophan is present in an amount less than about 5.0% by weight of the total amino -nitrogen, and (c) at least 1 gram per liter of an antioxidant system comprising beta-carotene, vitamin C, vitamin E and selenium (see claim 1). The reference teaches that the total amount of branched-chain amino acids ("BCAA") useful in the present invention is about 15-50 g/100 g protein (i.e. percent), preferably about 15-25 g/100 g. The reference teaches that the daily delivery of BCAAs is about 5-26 g. The reference teaches the branched-chain amino acids valine, leucine, isoleucine or mixtures thereof. Since there is 9.08 g of leucine and total of 19.75 g of BCAA, 9.08/19.75 is about 46% of the leucine in the BCAA. Since the reference teaches that the total amount of BCAA useful in the present invention is about 15-50 g/100 g protein, and there is 46% of leucine in the BCAA composition, this implies that there is about 23% of leucine.

Allen and Phillips teach the importance of leucine, isoleucine and valine in stimulating muscle growth. Vickery teaches that L-leucine is useful for lowering blood sugar, stimulating protein synthesis in muscle and wound healing of skin and bone.

Vickery teaches that L-valine aids in wound healing, muscle growth and liver diseases. L-valine is present in the composition in an amount of from about 7% to about 10% by weight, from about 8% to about 9% by weight. Vickery reference teaches a composition comprising about 6% to about 9% L-arginine, about 2% to about 4% L-cystine, about 1.5% to about 3.5% L-histidine, about 6% to about 9% L-isoleucine, about 8% to about 12% L-leucine, about 6% to about 8% L-lysine, about 2.5% to about 4.5% L-methionine, about 5.5% to about 7.5% L-phenylalanine, about 4.5% to about 6.5% L-threonine, about 4% to about 6% L-tyrosine, about 7% to about 10% L-valine, about 0.001% to about 0.03% by weight molybdenum, about 3% to about 30% by weight creatine monohydrate, and about 5% to about 45% by weight methylsulfonylmethane (see column 2, lines 8-30). When the least % of all components are added up, the molybdenum, creatine and methylsulfonylmethane would add up to about 10%. If there is about 7 to 9% L-valine, then there is about 7.8% (about 8%) L-valine based on the weight of total amino acids. Therefore, Vickery teaches the instant L-valine amount recited in the instant claims.

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings because all references teach nutritional compositions comprising differing amounts of protein and essential amino acids (such as leucine) for the same purpose (muscle enhancement). One of ordinary skill in the art would have been motivated to optimize the amount of leucine and valine in the composition, since Allen teaches that leucine, isoleucine and valine are three amino acids that stimulate muscle growth, Phillips teaches that leucine breaks down into HMB that build muscle, burn fat,

and increases in both muscle size and strengths, and Vickery teaches that L-leucine is useful in for lowering blood sugar, stimulating protein synthesis in muscle and wound healing of skin and bone. Vickery teaches that L-valine aids in wound healing, muscle growth and liver diseases. L-valine is present in the composition in an amount of from about 7% to about 10% by weight, from about 8% to about 9% by weight. One would be motivated to give leucine to produce the down-stream compound HMB and valine to aid in muscle growth. Again, Leu, Ile and Val are well known to be used for stimulating muscle growth. Vickery reference teaches a nutritional composition and composition for enhancing protein anabolism. It would have been obvious to one of ordinary skill in the art to optimize the different amino acid concentration, especially leucine and valine, since it is well known in the art that leucine, isoleucine and valine play an important role in muscle enhancement. As evidenced by the instant specification, the compositions of the instant application are for the promotion of muscle protein synthesis and control of tumor-induced weight loss in patients that are, for example, suffering from cancer cachexia (see abstract). Due to the loss of appetite due to cancer treatment, and due to appetite suppression, nutrition is necessarily a part of treatment process for improving patient's everyday life. For the process of improving and treating cancer and loss of appetite due to cancer, a nutritional requirement would be optimized and adjusted accordingly by those skilled in the art. Abbruzzese teaches that the therapeutic regimen will be developed to maintain and/or boost weight gain, giving motivation to optimize the nutritional content. From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in

producing the claimed invention. Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary. There is a reasonable expectation of success, since Salvati et al teach a kit that can comprise any agent, nutritional supplement for the treatment of cancer (prostate), and Hageman et al and Abbruzzese et al teach a nutritional supplement comprising essential amino acids that is useful in treating variety of diseases, including cancer. Both Allen and Phillips references were utilized to show the important role leucine plays in muscle enhancement. Vickery reference teaches the importance of L-valine and the composition comprising about 8 to about 12% leucine along with other amino acids.

It is known in the art that that supplements which stimulate muscle growth, include the three amino acids, leucine, isoleucine and valine. Furthermore, Phillips (1997) teaches that beta-hydroxy beta-methylbutyrate (HMB) is a metabolite of the essential amino acid leucine. Phillips teaches that HMB up-regulate the ability to build muscle and burn fat, and may help decrease stress-induced muscle protein breakdown, and enhance increases in both muscle size and strength. Therefore, one of ordinary skill in the art would have been motivated to optimize the concentration of different amino acids, specifically leucine, isoleucine and valine to stimulate muscle growth, to arrive at the optimal composition for the treatment of muscle enhancement for cancer patients.

Claims 1 and 23-25 are unpatentable over Heyland et al in view of Vickery reference.

Appellant argues that “Appellant has surprisingly found that a formulation containing free essential amino acids as compared to a formulation containing free essential and non-essential amino acids or intact protein is optimal…In addition, Appellant has surprisingly and unexpectedly found that particularly useful compositions for promotion of muscle protein synthesis or controlling tumor-induced weight loss, such as cachexia, e.g. cancer cachexia may be obtained by combining essential amino acids in free form and/or in salt form with intact protein." Appellant argues that “Heyland and Vickery fail to disclose or suggest compositions having leucine, valine in an amount of about 8% to about 10% by weight based on the weight of total amino acids, a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90 and wherein the ratio of leucine in free and/or salt form to leucine in form of the intact protein is about 3:1 to about 1:3 as required, in part, by independent claims 1 and 25. Heyland and Vickery also fail to disclose or suggest compositions consisting essentially of leucine in free and/or salt form, present in an amount of at least 30% by weight based on the weight of total amino acids, and valine in an amount of about 8% to about 10% by weight based on the weight of total amino acids, as required, in part, by independent claims 23 and 24." Appellant further argues that “Heyland discloses all essential amino acid and fails to recite any non-essential amino acids at any place in the disclosure…Heyland cannot

disclose or suggest a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.6 to about 0.9 as required, in part, by independent claims 1 and 25." Appellant further argues that "the present claims use the transitional phrase of "consisting essentially of," which limits the scope of a claim to the specific materials or steps and those that do not materially affect the basic or novel characteristics of the claimed invention...Therefore, with regard to the present claims, the "consisting essentially of" language limits the composition to containing leucine, valine and an essential amino acid (claims 1 and 23-24) or leucine, valine, an essential amino acid and an intact protein (claim 25), and those materials that do not materially affect the basic or novel characteristics of the claimed invention."

Appellant argues that "Vickery does not disclose or suggest compositions containing 8% to about 10% valine as required, in part, by the present claims…The amounts of valine disclosed in Vickery are not based on the weight of total amino acids, as is required, in part, by the present claims."

Examiner respectfully asserts that combined prior arts are *prima facie* obvious over the instant claims. As indicated in the rejection, Heyland et al teach a composition comprising 150 g technical leucine, and 180 g whey powder. Therefore, this implies that per 150 g of technical leucine, there is 97.5 g of leucine, 27 g of isoleucine, 3 g of valine and about 3 g of phenylalanine. Thus, 97.5 g leucine/180 g of whey protein gives 54.2% leucine. Vickery teaches that L-leucine is useful for lowering blood sugar, stimulating protein synthesis in muscle and wound healing of skin and bone. Vickery teaches that

L-valine aids in wound healing, muscle growth and liver diseases. L-valine is present in the composition in an amount of from about 7% to about 10% by weight, from about 8% to about 9% by weight. Vickery reference teaches a composition comprising about 6% to about 9% L-arginine, about 2% to about 4% L-cystine, about 1.5% to about 3.5% L-histidine, about 6% to about 9% L-isoleucine, about 8% to about 12% L-leucine, about 6% to about 8% L-lysine, about 2.5% to about 4.5% L-methionine, about 5.5% to about 7.5% L-phenylalanine, about 4.5% to about 6.5% L-threonine, about 4% to about 6% L-tyrosine, about 7% to about 10% L-valine, about 0.001% to about 0.03% by weight molybdenum, about 3% to about 30% by weight creatine monohydrate, and about 5% to about 45% by weight methylsulfonylmethane (see column 2, lines 8-30). When the least % of all components are added up, the molybdenum, creatine and methylsulfonylmethane would add up to about 10%. If there is about 7 to 9% L-valine, then there is about 7.8% (about 8%) L-valine based on the weight of total amino acids. Therefore, Vickery teaches the instant L-valine amount recited in the instant claims.

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of the prior arts because all references teach nutritional compositions comprising differing amounts of protein and essential amino acids (such as leucine) for the same purpose (muscle enhancement). One of ordinary skill in the art would be motivated to optimize the amounts of valine and isoleucine, since Vickery teaches that L-valine aids in wound healing, muscle growth and L-leucine is important in lowering blood sugar, stimulating protein synthesis in muscle and wound healing of skin and bond. Leu, Ile and Val are well known to be used for stimulating muscle growth.

Vickery teaches about 7% to about 10% of leucine along with other amino acid compositions.

In response to Appellant's argument that " Heyland discloses all essential amino acid and fails to recite any non-essential amino acids at any place in the disclosure…Heyland cannot disclose or suggest a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.6 to about 0.9 as required, in part, by independent claims 1 and 25", the claims do not recite that the composition requires non-essential amino acids. Claim 1 recites, "A composition comprising leucine, valine in an amount of about 8% to about 10% by weight based on the weight of total amino acids, and at least one essential amino acid…said composition provides a ratio of total essential amino acids to total amino acids ranging from about 0.60 to about 0.90" (claim 1) and "A composition consisting essentially of: a) leucine, valine in an amount of about 8% to about 10% by weight based on the weight of total amino acids, and at least one essential amino acid…b) at least one intact protein…wherein said composition provides a ratio of total essential amino acids and, optionally, conditionally essential amino acids..." (claim 25). The claim 25 recites that there is optionally conditionally essential amino acids. There is no requirement that non-essential amino acids must be present.

In response to Appellant's argument regarding "surprising and unexpected benefits of the claimed composition having optimal amount of leucine and essential amino acids," Appellant has not compared the results of the instant components to the components of prior arts. The specification discloses that protein synthesis in muscle in

Leu (25%) was 6.8 ± 1.1; Leu(35%) was 6.9 ± 0.6; Leucine alone was 6.6 ± 0.7. Protein breakdown in Leu (25%) was 8.1 ± 1.2; Leu (35%) was 8.0 ± 0.4; Leucine alone was 9.2 ± 0.5 (see Table 4). There is not much difference between Leu (25%) and Leu (35%) and Leu alone for protein synthesis. There is not much difference between Leu (25%) and Leu (35%) for protein breakdown.

Furthermore, Appellant has not defined what encompasses "consisting essentially of" in the specification. In fact the instant specification does not define the phrase "consisting essentially of". The MPEP states the following: "The transitional phrase 'consisting essentially of' limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. A 'consisting essentially of' claim occupies the middle ground between closed claims that are written in a consisting of' format and fully open claims that are drafted in a comprising' format...For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to 'comprising'" (see MPEP 2105). Therefore, claims 23-25 and 28 have been treated as "a composition comprising".

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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